REMARKS

Claims 1, 19, 22, 23 and 68-134 are currently pending in this application. Claims 92, 93, 95-97, 100, 101, 104 and 105 stand withdrawn. Claims 1, 19, 22, 23, 106, 107 and 112 are canceled herein without prejudice or disclaimer as to the subject matter therein. Applicants respectfully reserve the right to prosecute the subject matter of the canceled claims in one or more continuation or divisional applications. Claims 68, 73-77, 108, 113, 117-121, 124, 126 and 127 are amended herein. New claims 135-139 are presented for entry and consideration. Support for amended claim 108 can be found throughout the application as originally filed, *inter alia*, on page 17, line 25. Support for amended claim 113 can be found throughout the application as originally filed, *inter alia*, in canceled claim 1. Support for new claims 135-139 can be found throughout the application as originally filed, *inter alia*, in claims 19, 22, 23, 106 and 112. Upon entry of this response with amendments and new claims, claims 68-105, 108-111 and 113-139 will be pending.

Objections

Claims 118 and 125 were objected to as being dependent upon a rejected base claim. Applicants have amended the dependencies of claims 118 and 125, and in light of the other claim amendments set forth herein, believe that the Examiner's concerns have been addressed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the objection to claims 118 and 125, and request an indication of allowance thereof.

Allowed Claims

Applicants appreciate the Examiner's indication that claims 22, 23, 68-72, 80-91, 94, 98, 99, 102, 103 and 109-111 are allowed.

Rejections

Rejections under 35 U.S.C. § 112, 2nd Paragraph

Claims 73-79, 107, 113-117 and 119-123 were rejected under 35 U.S.C. § 112, 2nd paragraph as indefinite for allegedly failing to particularly point out and distinctly claim the

subject matter Applicants regard as the invention. The Office Action states that the recitation of "trimeric polypeptide complex" in claim 74 lacks antecedent basis in claim 1. The Office Action also states that it is unclear how claim 107 further limits claim 90 in the recitation of "further processing". Additionally, the Office Action states that claims 73, 75-79, 113-117 and 119-123 are vague and indefinite for reliance on a Figure in the disclosure.

Applicants have amended claims 73-77, 113, 117 and 119-121, and believe that the Examiner's concerns have been addressed. Furthermore, claim 107 is canceled herein without prejudice or disclaimer as to the subject matter of claim 107. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 73-79, 113-117 and 119-123 under 35 U.S.C. § 112, 2nd paragraph.

Rejections under 35 U.S.C. § 112, 1st Paragraph

Claims 108 and 127 were rejected under 35 U.S.C. § 112, 1st paragraph as allegedly failing to comply with the written description requirement. Applicants have amended claims 108 and 127 herein, and believe that the Examiner's concerns have been addressed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 108 and 127 under 35 U.S.C. § 112, 1st paragraph.

Rejections under 35 U.S.C. § 102

Claims 1, 19, 112, 124, 126, 131, 132 and 134 were rejected under 35 U.S.C. § 102 (b) as allegedly anticipated by the disclosure of Forsburg *et al* (Gene, June 3, 1997, Vol. 191, pp. 191-195) as evidenced by Chen *et al* (Biochemistry, 1998, vol. 37, pp. 13643-13649) and Kim *et al* (Biochemistry, 1996, Vol. 35, pp. 5359-5365) and Nautiyal *et al* (Biochemistry, 1995, Vol. 34, pp. 11645-11651).

Applicants respectfully disagree and traverse this rejection.

In order for a reference to anticipate under 35 U.S.C. § 102(b), the reference must disclose all elements of the claimed invention in a printed publication in this or a foreign country more than one year prior to the date of application for patent in the United States. *See* MPEP § 2133.

Applicants respectfully note that claims 1, 19 and 112 are canceled herein, and claim 113 is amended to require (in part) that the claimed monomer polypeptide construct comprise at least one tetranectin trimerising structural element (TTSE) wherein said TTSE is a

polypeptide having at least 68% amino acid sequence identity with the consensus sequence shown in SEQ ID NO:40. The remaining rejected claims depend from claim 113. Applicants submit that Forsburg *et al* do not teach a monomer polypeptide construct comprising at least one tetranectin trimerising structural element (TTSE) wherein said TTSE is a polypeptide having at least 68% amino acid sequence identity with the consensus sequence shown in SEQ ID NO:40.

Because Forsburg *et al* do not disclose all elements of the claimed invention, Forsburg *et al* cannot stand as anticipatory art under 35 U.S.C. § 102(b). Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections of claims 124, 126, 131, 132 and 134 under 35 U.S.C. § 102 (b) as allegedly anticipated by Forsburg *et al.*

Rejections under 35 U.S.C. § 103

(**A**) Claims 1, 19, 106, 112, 124, 126, 127, 129 and 131-134 were rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Pack *et al* (WO 96/37621) in view of Nautiyal *et al.* The Office Action states that Pack *et al* teach peptidic multimerization devices providing for the targeted multimerization of enzymes, toxins, cytokines, kinases, phosphatases, lectins, peptidic hormones, cell adhesion proteins, metal binding domains, peptidic vaccines, bioactive peptides or soluble cell-surface proteins. According to the Office Action, Pack *et al* do not specifically teach multimerization devices which are capable of forming an alpha helical coiled coil trimer which remains a trimer up to at least 60 degrees C. The Office Action also states that Nautiyal *et al* teach a heterotrimeric coiled coil comprising a heptad repeat wherein positions "a" and "d" are occupied by hydrophobic amino acid sequences, and three monomer polypeptides which were designed to form the coiled coil. The Office Action states that Nautiyal *et al* teach that a mixture comprising equimolar concentrations of each peptide was fully helical and remained trimeric until 87.5 degrees C, thus fulfilling the specific embodiments of claim 1 regarding temperature stability at 60 degrees C.

The Office Action therefore holds that it would have been *prima facie* obvious at the time the claimed invention was made to use the ABC peptides of Nautiyal *et al* as an autonomous oligomerization domain in the peptidic multimerization devices taught by Pack *et al*, and that one of skill in the art would be motivated to do so by the teachings of Pack et al

on the requirement that the small, peptidic multimerization devices which at least form trimers.

Applicants respectfully disagree and traverse this rejection.

In order to establish a *prima facie* case of obviousness, three basic criteria must be met.

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.

See MPEP §§ 2142, 2143.

Applicants submit that there is no suggestion or motivation to modify the teachings of Pack *et al*, or to combine the teachings of Pack *et al* and Nautiyal *et al*, to obtain the claimed invention. Furthermore, Applicants submit that Pack *et al*, alone or in combination with Nautiyal *et al*, do not teach or suggest all of the elements of the rejected claims. Rejected claims 1, 19, 106 and 112 are canceled herein without prejudice or disclaimer as to the subject matter of those claims. The remaining claims rejected in this section now depend from amended claim 113.

As noted *supra*, claim 113 (now independent claim 113) is amended herein to require (in part) that the monomer polypeptide construct comprise at least one tetranectin trimerising structural element (TTSE), wherein the TTSE is: a polypeptide having at least 68% amino acid sequence identity with the consensus sequence shown in SEQ ID NO:40; covalently linked to at least one heterologous moiety; and capable of forming a stable triple alpha helical coiled coil complex with two other TTSEs, wherein said complex remains as a trimer at a temperature of at least 60 degrees C.

The Office Action states that Pack *et al* "do not specifically teach multimerization devices which are capable of forming an alpha helical coiled coil trimer which remains a trimer up to at least 60 degrees C". *See* Office Action, Page 6, lines 13-15. Applicants submit that there is no suggestion or motivation to modify the teachings of Pack *et al*, or to

combine the teachings of Pack *et al* and Nautiyal *et al*, to obtain all of the elements of the claimed invention.

Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 124, 126, 127, 129 and 131-134 under 35 U.S.C. § 103(a).

(**B**) Claims 1, 19, 106, 112, 124, 126, 127 and 129-134 were rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Pack *et al* (WO 96/37621) and Nautiyal *et al*, in further view of Hoppe *et al* (WO 95/31540). The Office Action states that Hoppe *et al* teach monomer polypeptide constructs comprising heterologous moieties such as carbohydrates, lipid-containing structures and DNA or RNA derivatives, which fulfill the specific embodiments of claim 130. The Office Action states that it would have been *prima facie* obvious at the time the claimed invention was made to use the heterologous moieties taught by Hoppe *et al* in the monomer polypeptides rendered obvious by the combination of Pack *et al* and Nautiyal *et al*, and that one of skill in the art would have been motivated to do so because both of Pack *et al* and Hoppe *et al* disclose the delivery of heterologous molecules by means of a multimerization unit.

Applicants respectfully disagree and traverse this rejection.

Rejected claims 1, 19, 106 and 112 are canceled herein without prejudice or disclaimer as to the subject matter of those claims. The remaining claims rejected in this section now depend from amended claim 113.

As noted *supra*, claim 113 (now independent claim 113) is amended herein to require (in part) that the monomer polypeptide construct comprise at least one tetranectin trimerising structural element (TTSE), wherein the TTSE is: a polypeptide having at least 68% amino acid sequence identity with the consensus sequence shown in SEQ ID NO:40; covalently linked to at least one heterologous moiety; and capable of forming a stable triple alpha helical coiled coil complex with two other TTSEs, wherein said complex remains as a trimer at a temperature of at least 60 degrees C.

Applicants submit that there is no suggestion or motivation to modify the teachings of Pack *et al*, or to combine the teachings of Pack *et al* and Nautiyal *et al*, to obtain all of the elements of the claimed invention, and that the disclosure of Hoppe *et al* does not remedy the deficiencies of the disclosures of Pack *et al* and Nautiyal *et al*.

Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 124, 126, 127 and 129-134 under 35 U.S.C. § 103(a).

(C) Claims 1, 19, 106, 112, 124, 126-129 and 131-134 were rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Pack *et al* (WO 96/37621) and Nautiyal *et al*, in further view of Schlom (In: The Molecular Basis of Clinical Oncology, 1991, pp.95-144). The Office Action states that Schlom teaches that monoclonal antibodies can be used to deliver the toxin ricin to cancer cells, and that Schlom also teaches the use of scFv for targeting cancer cells in vivo. According to the Office Action, claim 128 embodies the monomer polypeptide of claim 126 wherein the toxin is ricin.

The Office Action states that it would have been *prima facie* obvious at the time the claimed invention was made to include in the heterotrimer rendered obvious by the combination of Pack *et al* and Nautiyal *et al*, a monomer peptide of ABS conjugated or fused to ricin, and a monomer peptide comprising the scFv1-linker1-trimerization unit-linker2-scFv2 domains, and that one of skill in the art would have been motivated to do so by the teachings of Nautiyal *et al* on the ability of the ABS trimer to associate three different proteins, and the teachings of Schlom on the targeting of cancer cells by scFv and the killing of cancer cells by the administration of ricin conjugated to monoclonal antibodies.

Applicants respectfully disagree and traverse this rejection.

Rejected claims 1, 19, 106 and 112 are canceled herein without prejudice or disclaimer as to the subject matter of those claims. The remaining claims rejected in this section now depend from amended claim 113.

As noted *supra*, claim 113 (now independent claim 113) is amended herein to require (in part) that the monomer polypeptide construct comprise at least one tetranectin trimerising structural element (TTSE), wherein the TTSE is: a polypeptide having at least 68% amino acid sequence identity with the consensus sequence shown in SEQ ID NO:40; covalently linked to at least one heterologous moiety; and capable of forming a stable triple alpha helical coiled coil complex with two other TTSEs, wherein said complex remains as a trimer at a temperature of at least 60 degrees C.

Applicants submit that there is no suggestion or motivation to modify the teachings of Pack *et al*, or to combine the teachings of Pack *et al* and Nautiyal *et al*, to obtain all of the

elements of the claimed invention as amended herein, and that the disclosure of Schlom does not remedy the deficiencies of the disclosures of Pack *et al* and Nautiyal *et al.*

Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 124, 126-129 and 131-134 under 35 U.S.C. § 103(a).

CONCLUSION

An indication of allowance of all claims is respectfully solicited. Early notification of a favorable consideration is respectfully requested. In the event any issues remain, Applicant would appreciate the courtesy of a telephone call to their counsel to resolve such issues and place all claims in condition for allowance.

Respectfully submitted,

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Dated: September 12, 2005

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